REMARKS

Status of the Claims

Claims 7-9 are pending in this application.

The Claims Rejections Under 35 U.S.C. § 112, 1st ¶, Enablement, Should Be Withdrawn

Claims 7-9 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly nonenabled. Applicants respectfully traverse.

The rejection should be withdrawn for two overarching reasons: (1) The Office's claim construction is legally incorrect; and (2) the rejection is founded on statements of fact that are either conclusory or contradicted by the evidence of record.

Reason (1): Incorrect Claims Construction. The rejection mis-construes the claims as if they recite an endpoint of tumor reduction. Applicants have brought this erroneous construction to the attention of the Office without avail. None of the claims group currently under examination by the Office ever recited "treating cancer," "cancer treatment," "tumor reduction," or the like, nor do any of the currently pending claims recite "treating cancer," "cancer treatment," "tumor reduction," or the like. The independent claim actually reads:

> A method of inducing an immunoresponse in a human or non-human animal comprising administering a peptide fragment of SEQ ID NO:2 to the human or non-human animal, wherein the peptide fragment comprises SEQ ID NO:25.

Essentially, the Office is improperly reading a tumor reduction limitation into the claims.

Applicants brought to the Office's attention MPEP § 2107.02, which prohibits reading into the claim limitations that are not there. Nonetheless, the Office states

> The claims are reasonably interpreted as a method for treating cancer, such as **reduction of cancer cell growth** in vivo, as contemplated in the specification, via inducing an immune response. The specification contemplates testing the effect of the stimulated T cells on tumor cells transfected with cDNA encoding SEQ ID NO:2 (p.64, last two paragraphs, bridging p.65).

See the Office Action dated 5 Mar 08 (emphasis added). This statement makes it abundantly clear that the Office is not utilizing the specification to interpret a term or clause in the claims. Rather, it is reading a limitation into the claims from text found in

the specification. Moreover, the cited portion of the specification is the Examples section. One of the Examples does relate to experiments that can be carried out to identify T-cells that specifically react to the polypeptide of SEQ ID NO:2. But there is no basis in patent law to read subject matter from the examples into a claim, as has been done here. (It is worth noting that one of the other examples--Example 10--actually discloses the induction of an immune response to a peptide comprising SEQ ID NO:25.)

Due to of the Office's erroneous claim construction, the remainder of the rejection is ill-founded because it does not relate to whether Applicants have enabled methods of inducing an immunoresponse. Applicants maintain that their methods are enabled. Supporting data can be found in the Examples (see, e.g., Example 10, in which a cell mediated response to the peptide recited in claim 7 is demonstrated; see also, Examples 12 and 17, which demonstrates that other disclosed peptides also induce an immune response, namely a specific antibody response in rabbits). The rejection of claims 7-9 should be withdrawn because it is based upon an incorrect claim construction.

As shown above, the claims construction improperly reads a limitation into the claims. The rejection should be withdrawn for this reason.

Reason (2): Incorrect and/or unsupported factual findings. The rejection also makes numerous allegations of fact relating to the state of the art or the methods disclosed in Applicants' specification. Generally, these findings are either unsupported by evidence and therefore conclusory, or they are contradicted by the evidence of record. The remaining paragraphs of this section deal with each of these allegations.

First, the Office makes general allegations regarding the state of the art of cancer therapeutics, relying upon Kirkin, Boone, Gaiger, Ezzell, and Spitler (of record). Applicants submitted a reference that rebuts Gaiger. (See the Response, dated 18 Jul 07, discussing Oka *et al*. which demonstrates that WT-1 peptides are immunogenic and effective in vivo.) The rest of these references are irrelevant because of their age: Kirkin, Boone, Ezzell, and Spitler were published in the 1990s. It is elemental that a "state of the art" reference must bear some relevance to the state of the art at the time

of an application's priority. Thus, even if the inquiry into the state of the art of cancer therapeutics were relevant to the present rejection, the Office's findings regarding the state of the art are relevant only to a time in the 1990s.

The Office also alleges that one of skill in the art would not accept that a CTL response or antibody response could be induced in a cancer patient using a fragment of SEQ ID NO:2 comprising SEQ ID NO:25, relying for support on Smith, Boone, and White (discussing immunosuppression and immune tolerance in cancer). Smith and Boone are mainly of interest in a historical sense, dating from 1994 and 1992, respectively. White *et al*. was first mentioned in the Office Action dated mailed 27 Oct 2006 for the proposition that immunotherapy is unpredictable because of the possibility of antigen internalization. But White does not relate to the cancer antigen of Applicants' disclosure, namely CASB7439/ASCL2/HASH2, and White is therefore irrelevant to whether CASB7439/ASCL2/HASH2 would be internalized in a cancer cell.

Nonetheless, the Office has continued to rely on White, stating "one cannot predict the behavior of an antigen unless tested." But Applicants *have* tested their antigen and the evidence of record favors a conclusion that ASCL2/HASH2 protein (i) is over-expressed on cancer cells, not normal cells, and (ii) is not internalized. See Example 11, which demonstrates by immunohistochemistry that CASB7439/ASCL2/HASH2 staining is high in colon cancer and low in normal colon. These results favor a conclusion that CASB7439/ASCL2/HASH2 protein is present on the surface of colon cancer cells (because it is accessible to staining).

Despite the lack of evidence to support its position, the Office maintains that "[o]ne cannot predict that the claimed antigen is not internalized or downregulated in cancer cells, in view of the teaching of White et al." But the Office's arguments based upon White are revealed as speculative and unsupported when considered in light of Applicants' evidence (above). Applicants have invited the Office to provide an affidavit pursuant to 37 CFR 1.104(d)(2) to support its argument, but none has been forthcoming. Applicants wish to emphasize that the weight of the evidence of record supports Applicants' position.

The Office next states that "[t]he specification however does not have any objective evidence of **successful treatment of cancer**...", discounting Applicants' supporting data on the grounds that "[t]he specification only discloses that a peptide fragment comprising SEQ ID NO:25 in vitro activates T cells from PBMC of 3 healthy donors, which T cells recognize DCs pulsed with full length SEQ ID NO:2...." As an initial matter, even if the claims under examination were drawn to methods of treating cancer, the Office's requirement of a *successful cancer therapeutic* would be an inappropriately high standard for enablement. See *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995)(requiring information of the sort necessary for regulatory approval not an appropriate standard by which to judge patentability). Moreover, the Office's treatment of Applicants' supportive data fails to properly weigh and balance the evidence of record. Essentially, Applicants have provided actual evidence that the specific peptide of SEQ ID NO:25 induces a cell mediated immune response and there is no contrary evidence of record. Thus, the evidence of record favors a conclusion that a fragment comprising SEQ ID NO:25 would induce an immune response.

For the reasons stated above, the weight of the evidence of record supports Applicants position regarding the disputed facts. Because of the lack of factual support, the rejection of claims 7-9 must be withdrawn.

Miscellaneous. Applicants have pointed out that the Office's improper claim construction harms Applicants because by limiting the claims to therapeutic methods, the Office fails to consider other *bona fide* uses for Applicants' claimed methods for inducing an immunoresponse. Applicants have disclosed that their methods can be used "to generate antibodies or reagents specific for the polypeptide of the present invention, as diagnostic reagents to detect...genetic or biochemical markers in blood or tissues that will enable the detection of very early changes along the carcinogenesis pathway will help in determining the best treatment for the patient." See US20050260634, paragraphs [0182]-[183]. Those of skill in the art understand that

such "surrogate tumor markers" can be used to diagnose and stage different forms and states of cancer. See paragraph [0183]. For example, one could easily use these markers to compare the expression of a particular gene between a diseased tissue and a normal tissue. See paragraph [0184]. The comparison can be made at the protein level. See paragraph [0188]. Those of skill in the art can also easily detect tumor marker expression levels and subcellular localization by using antibodies to the corresponding protein. See paragraph [0200]. Antibodies for use in the method are easy to make and can be obtained by administering the polypeptides or epitope-bearing fragments to an animal, which may be a non-human animal, using routine protocols. Thus, one utility for the products of the presently claimed methods (inducing an immune response) would be the use of these products (such as antibodies) to detect a tumor marker (CASB7439/ASCL2/HASH2). Applicants emphasized that this utility has not been considered due to the Office Action's improper claim construction. In response, the Office states that

> "Applicants argue limitation[s] not in the claim. The claims are not drawn to a method for diagnosis of cancer, by inducing an immune response."

The Office's response appears to take the position that the use need not be considered unless it is expressly recited in the claim, but there is no support for such a proposition. Indeed, it is a well-understood tenant of patent law that the claims themselves need not recite any utility (only the specification must describe a utility). Thus, the Office's failure to consider the utility described above cannot be supported and the rejection of claims 7-9 should be withdrawn for this reason, as well.

Claim 9. Applicant also requests clarification for the rejection of claim 9. In the Advisory Action which preceded the present Office Action, the Office stated that "[t]he claims do not recite the use of adjuvants with SEQ ID NO:25...." See the Advisory Action dated 4 Sep 2007, page 5, third full paragraph. Applicants' representative drew the Office's attention to claim 9, which expressly recites adjuvants. In the present rejection, the Office now states that "there is no evidence that the claimed peptide has a

synergistic effect on the added adjuvants, concerning cancer treatment." Applicants can find no reason for the Office to require a showing of synergy and no basis in the Rules has been cited for this requirement. Applicants respectfully request that this separate rejection of claim 9 be withdrawn.

CONCLUSION

In view of the remarks herein above, Applicants respectfully submit that the rejection of claims 7-9 is overcome. In particular, Applicants have demonstrated the following: (1) That the claims construction improperly reads a limitation into the claims. (2) That the weight of the evidence of record supports Applicants position regarding the disputed facts. For these reasons, the rejection of claims 7-9 should be withdrawn. Early notice to the effect that this application is now in condition for allowance is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge any fees or credit any overpayment particularly including any fees required under 37 CFR §1.16 or 1.17, and any necessary extension of time fees, to Deposit Account No. 07-1392.

Respectfully submitted,

/Eric J. Kron/
Eric J. Kron
Attorney for Applicants
Registration No. 45,941

Date: 5 Aug 2007
GlaxoSmithKline
Five Moore Drive, PO Box 13398
Research Triangle Park
North Carolina 27709
Telephone: (919) 483-8961
Facsimile: (919) 483-7988